STUDIES IN BLACKWATER FEVER

(1) STATISTICAL

BY

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In this paper I propose to consider some of the facts bearing on the malarial origin of blackwater fever which I have been able to collect from an examination of recent literature.

Arguments of a general nature, though there are many, I shall not consider here, but shall examine the facts so far as I have been able to ascertain them under the following headings:—

(1) Malaria parasites.
(2) Pigmented leucocytes.
(3) Post-mortem examinations.
(4) Influence of malaria.
(5) Relationship to species of malaria parasite.
(6) Effect of period of residence.
(7) Seasonal prevalence.
(8) Correlation between malaria and blackwater statistics.
(9) Second attacks.

In 1901, Christophers and myself (1901), as a result of our microscopical studies of blackwater fever, came definitely to the conclusion that blackwater is malarial in origin but is not simply an attack of malaria, but occurs only in those who are in a condition induced by repeated malarial infection lasting over a certain time.

MALARIA PARASITES

One of the most important facts, in my opinion, bearing on the aetiology of blackwater fever is the presence of malaria parasites in the blood of blackwater cases. In the literature I have been able to collect 390 cases. I divide them into three categories, those on the day before, those on the day of, and those on the day after the onset of blackwater, as in the accompanying Table I. My reason for doing this is that in my experience, and also in that of others, parasites when found rapidly disappear.

TABLE I

Author	Day before onset of hemoglobinuria		Day of onset of hemoglobinuria		Day after onset of hemoglobinuria		Remarks
	No. of cases	No. positive	No. of cases	No. positive	No. of cases	No. positive	
Barratt & Yorke (1909)	2	1	5	0	7	0	
Brault (1903)	—	—	1	1	—	—	It is not clear whether 'day of' or 'day after.'
Brem (1906)	1	1	1	0	1	0	Cases 10 and 13; for other cases see Deeks & James.
Capogrossi (1910)	—	—	1	1	1	0	S.T. parasites present on 1, 4, 7, and 8th day.
Cardamatis (1911)	—	—	15	0	4	2	
Carducci (1907)	—	—	1	1	1	1	Bl. pos. on 1, 2nd day, neg. on 3, 4, 5th day, death.
Christophers & Bentley (1908)	—	—	10	6		—	
da Costa (1906)	2	2	12	10	19	10	
Deaderick (1907)	—	—	4	1	2	0	
Deeks & James (1911)	28	14	36	12	42	7	
Frere (1910)	—	—	1	1	1	0	
Gastou & Dufougeré (1911)	—	—	1	1	—	—	Not clear whether 'day of' or 'day after.' 10 c.cm. blood centrifugalised and crescents found.
German East Africa (1909-10)	1	1	2	2	2	1	
Grattan (1907)	—	—	1	0	2	1	
Jungels (1911)	—	—	1	0	1	0	
Kleine (1901)	2	2	2	1	1	0	

TABLE I—*continued*

Author	Day before onset of hemoglobinuria		Day of onset of hemoglobinuria		Day after onset of hemoglobinuria		Remarks	
	No. of cases	No. positive	No. of cases	No. positive	No. of cases	No. positive		
Krauss (1904)	—	—	—	—	1	0		
Külz (1908)	—	—	—	—	1	0		
Külz (1910)	—	—	—	—	1	1		
Marshall (1910)	—	—	—	—	1	0		
Masterman (1906)	—	—	—	—	1	1		
da Matta (1912)	2	1	1	0	—	—		
O'Donoghue (1912)	1	1	1	0	1	0		
Orme (1908)	—	—	—	—	1	1		
Otto (1902)	1	1	1	0	1	0		
Powell (1898)	2	2	—	—	—	—		
Römer (1911)	—	—	—	—	1	0		
Ross, Thomson & Simpson (1910)	1	0	1	0	1	0		
Ruge (1902)	1	1	1	1	1	0		
Stephens (1903)	23	22	63	39	64	11		
Whipple (1909)	—	—	—	—	2	1		
							Total cases	Positive
	67	49	162	77	161	37	390	163
	73%		47·5%		23%		41·8%	

This means that in 100 cases of blackwater examined on the day before the onset, parasites will be found in 73 cases, in 100 cases examined on the day of onset in 47·5* and in 100 cases examined on the day after in 23.†

An important deduction that I think may safely be made from these figures is that parasites disappear, and indeed rapidly, during the course of the disease, as we had observed in our original studies. This disappearance of parasites is in all probability associated with the acute haemolysis that is taking place in blackwater fever, and *should be borne in mind in all comparisons* between the parasite rates in blackwater fever and malaria.

Further, the fact that on the day before the onset of the blackwater parasites are found in 73% of cases seems to point to the initial attack being closely associated with a malarial attack. That relapses do occur during the course of the disease (which relapses in some cases at least can be brought on by quinine) without the occurrence of parasites in the blood, seems to be certain, though I have not collected the data on the subject. And even if parasites were rarely found in blackwater, it would not necessarily exclude its malarial origin, because it might be that it was just in the chronic cases of malaria where parasites are absent or scanty that blackwater occurred, but I will not pursue the argument further, as I wish as far as possible in this paper to ascertain facts and avoid discussion.

The following table, compiled from Panse's (1902) cases, 35 in number, enables one to show in more detail how time affects the result of the examination for parasites in blackwater:—

TABLE IA

Time of blood examination	Cases	Positive	Percentage
Day before onset	9	8	88·9
Day of onset (*a*) before onset	11	8	72·7
,, (*b*) after onset	11	6	54·5
Within 12 hours after onset	12	6	50·0
More than 12 hours after onset	31	9	29·0

* A correction is probably necessary for those cases occurring on the day *of* the blackwater for some of these will probably have been examined *before* the onset of the blackwater and some (probably the majority) after, so that on the assumption that the parasite rate before the onset and that of the day before is the same, this figure should be reduced, but it is impossible to say by how much.

† Or put in a different way of 100 *positive* cases, 51 will occur on the day before, 32·8 on the day of, and 16 on the day after the blackwater.

The next tables, Table II and III, I give separately, as the data were compiled in a different way to that in Table I.

Table II.—Parasites in Blackwater Fever. Compiled from Deeks and James (1911)

75	cases examined	4 — 1 days *before* onset ...	Pos.	48	= 64·0 %
28	.. ..	1 day *before*	..	14	= 50·0 %
36	.. ..	*day* of *onset*	..	12	= 33·3 %
62	.. ..	1 — 4 days *after onset* ...	..	12	= 19·4 %
40,928	.. of	Malaria examined on admission ...	..	23,410	= 57·2 %
260	..	Amoebic dysentery	..	48	= 18·5 %
70	..	Liver abscess	..	7	= 10·0 %
33	..	Typhoid	..	4	= 12·1 %
— ?	..	Tuberculosis		About	12·0 %
— ?	..	Pneumonia		Less than	12·0 %

Table III

Madeira-Mamore Railway Co., Porto Velho, Brazil. Compiled from Lovelace (1913)

	Total blood-examinations (26 months)	Positive	Rate
Malaria	16,434	9,155	55·7 %
Blackwater*	383	178	46·5 %

The tables are also of value because we are able to compare the percentages in blackwater with those made in malaria under the same conditions of observer, staining, and probably of time devoted to each examination.

In the next table, Table IIIA, the data of the first three tables are summarized.

From it we see that parasites are found in blackwater fever in 42·9% of cases (taking no account of the day of the disease on which the examination is made), while in malaria, parasites are found in 56·8% of cases. If we accept the conclusion drawn from Table I, viz., that parasites disappear during the course of the

* In the majority of cases only one blood examination was made, and it was made during the period of haemoglobinuria.

disease, the lower percentage in blackwater is readily accounted for. The figure for malaria is probably low, but in the Panama figures of Deeks and James it should be remembered that only a single examination was made on admission to hospital.

Table IIIa.—Parasite Rate in Blackwater Fever and Malaria

Cases	Positive	%	Observer
Blackwater Fever			
390	163	41·8	Various observers (Table I)
230	89	38·7	Deeks & James (1911)
383	178	46·5	Lovelace (1913)
1003	430	42·9*	
Malaria			
40,928	23,410	57·2	Deeks & James (1911)
16,434	9,155	55·7	Lovelace (1913)
57,362	32,565	56·8	

The objection has been brought against figures of this kind that in a malarial country parasites would be found in the same or about the same percentage in people not suffering from blackwater fever, but such objections have *not* been supported by actual data.

Christophers and myself (1901), moreover, examined 44 Europeans at Lagos, taken at random. They were especially from communities suffering much from malaria. We found parasites in 2, pigmented leucocytes in 2, i.e, 4 infected out of 44, about 9%.

Christophers and Bentley (1908) examined 66 babus in the Duars, Bengal, and found parasites or pigment in 14, i.e., 21·2%. In 10 cases of blackwater on the day of onset they found parasites or pigment in 8, or 80%. Further we have the control figures of Table II.

* This figure represents the positive parasite rate irrespective of the day of the disease and should be compared with the figures of Tables I and II.

If, then, these data are correct, they imply that in the general population and those suffering from diseases other than malaria or blackwater fever the parasite rate is not comparable with that in blackwater fever.

Moreover, I believe we are justified in meeting the above objection more forcibly still. We have in blackwater a disease in which immediately before the onset of the disease malaria parasites are found in 73% of cases, taking the figure of Table I. If this does not signify that the disease is malarial, then the finding of parasites in 73% of cases of 'malaria' has also no significance, and 'malaria' is also due to some unknown cause.

PIGMENTED LEUCOCYTES

In blackwater fever it is the general experience that parasites when found rapidly disappear. We still, however, have a means of detecting a malarial infection if present, viz., by means of pigmented leucocytes. In the literature most frequently no statement is made with regard to pigmented leucocytes. The following figures of Christophers and Bentley are small and only suggestive, and more observations are required.

Table IV.*—Pigmented Leucocytes in Blackwater Fever (Christophers & Bentley, 1908).

	First Day		Second Day		Fourth-Sixth Day	
	No. of cases	No. positive	No. of cases	No. positive	No. of cases	No. positive
Parasites	10	6	7	2	10	1
Pigment	10	8	7	6	10	4

POST-MORTEM EXAMINATIONS

In 31 cases where definite statements positive or negative have been made malaria pigment was found P.M. in 26, i.e., 83·9%. The evidence of malaria then in 5 cases is negative. If the absence of pigment P.M., supposing the facts correct, definitely excludes malaria then some blackwater cases must be due to other causes, which one must admit is not impossible, although I believe the facts prove that malaria is the dominant factor.

* In this table, the data are obtained from the same 10 cases.

TABLE V.—Post-mortem Records of those cases only where definite statement made.

Cases	Parasites or pigment positive	Negative	Authority
3	0	3	Barratt & Yorke (1909). But in one of these scanty pigmented leucocytes, found during life.
6	6	0	H. Werner (1907).
13	13	0	G. H. Whipple (1909).
2	2	0	Christophers & Bentley (1908).
5	5	0	Stephens & Christophers (1901). (B.W. cases IX-XVI, p. 24.)
2	0	2	Brem (1906). In one case only a smear from a rib examined.
31	26	5	
	83·9 %	16·1 %	

INFLUENCE OF MALARIA

The influence of malaria in determining blackwater is shown in a different way by the following table compiled from Deeks and James.

TABLE VI.—Influence of Malaria. Ancon Hospital, July, 1904—Sept., 1910.

Among 40,928	cases diagnosed as Malaria,
102	cases of Blackwater developed subsequent to admission.
Among 42,000	cases diagnosed as Typhoid, Pneumonia, Amoebic dysentery, and Tuberculosis, etc. (medical and surgical).
4	cases of Blackwater developed subsequent to admission.*

RELATIONSHIP TO SPECIES OF MALARIA PARASITE

The statistics on this point are often fallacious. What we require to know is not the percentage of malignant tertian or other species of parasite in blackwater cases, but rather what number of blackwater cases there is in 100 cases of malignant tertian, simple tertian and quartan respectively. The following figures show this.

* In the surgical wards: 3 after well defined malarial paroxysms, 1 after quinine in a patient with a history of much malaria.

TABLE VII.—Compiled from Deeks & James (1911)

	Of 23,410 positive malaria cases	Of 89 positive blackwater cases	Ratio of blackwater % to malaria %	Ratio of M.T. to S.T.
Malignant Tertian	74 %	76·4 %	103·2 %	100
Simple Tertian	26 %	23·6 %	90·8 %	88

i.e., if x cases of malignant tertian malaria give 100 cases of blackwater.
then x ,, simple ,, ,, ,, 88 ,, ,,

Compiled from Lovelace (1913)

	Of 9,155 positive malaria cases	Of 178 positive blackwater cases	Ratio of blackwater % to malaria %	Ratio of M.T. to S.T. and to M.T. & S.T. respectively
Malignant tertian	5988 = 65·4 %	87 = 48·9 %	74·8 %	100
Simple tertian	2760 = 30·1 %	74 = 41·6 %	138·2 %	185
M.T. + S.T.	391 = 4·3 %	17 = 9·6 %	223·3 %	299
Quartan	16 = 0·2 %	0 = 0·0	0·0	0

i.e., if x cases of malignant tertian malaria give 100 cases of blackwater.
then x ,, simple ,, ,, ,, 185 ,, ,,
and x ,, M.T. + S.T. ,, ,, 299 ,, ,,
and x ,, quartan ,, ,, 0 ,, ,,

The discrepancy between these two results I cannot at present explain, assuming they are both correct, but it should be noted that Lovelace (1913) in his paper states that the simple tertian parasite 'is here an extremely persistent infection. More time and more quinine are required for its eradication than for that of the aestivo-autumnal parasite.' And again he speaks of 'the rapid blood destruction in, the great prostration incident to, and the diabolical persistence of tertian infections.' It would seem as if here we had an example of increased virulence of the simple tertian parasite. One's own clinical experience of the malignant tertian parasite in the tropics and in temperate zones, seems certainly to point to differences in virulence.

INFLUENCE OF PERIOD OF RESIDENCE

There is a general impression that blackwater is most prevalent in the second or third year of residence, but the statistics on this point are nearly all subject to the objection that no account has been taken of the number of people in each residential period, first, second, third, etc., years, and this may vary much from year to year. Here again, what we require to know in the first place is not out of one hundred cases of blackwater how many occur in the first, second, etc., years, but how many cases of blackwater occur in each one hundred people or similar sample of the different periods of residence, one, two, three, etc., years. Knowing this, we can then calculate how many out of one hundred cases of blackwater occur in the first, second, third, etc., years. Plehn (1901) is the only observer who supplies us with what we require to know, though, unfortunately, his figures extend only to two years.

The figures in the second row of Table VIII indicate the number of people in their first, second, third, etc., month of residence under observation (for Hgb. estimations). Thus in the second month of residence there were seventy-five, therefore eight of these were not under observation in their first month, but whether the remaining sixty-seven were the same people as the sixty-seven in their first month, the table does not tell us; probably they were, and at the end of twenty-four months they were reduced to five, but it is not a material point.

Table VIII.—Blackwater Fever: Effect of Residence (Plehn, 1901).

First Year

Month...	1	2	3	4	5	6	7	8	9	10	11	12
Residents	67	75	75	71	67	62	61	57	55	50	46	47
Malaria cases	28	50	60	42	41	43	38	44	37	33	26	24
B.W. cases	0	0	0	0	0	3	4	6	3	4	1	1

SECOND YEAR

Month...	13	14	15	16	17	18	19	20	21	22	23	24
Residents	42	42	37	35	33	25	21	17	12	10	9	5
Malaria cases	21	29	18	9	13	12	7	9	1	3	1	4
B.W. cases	1	4	2	0	1	1	0	1	0	0	0	2

TABLE VIII. B. (compiled from previous table.)

Time of Residence	First 6 months	First year	Second year
Number of residents	69·5	61·1	24
Cases of blackwater	3	22	12
B.W. rate per 100 residents	4·32	36·0	50·0
Of 100 cases of B.W. there occur	5·02	41·86	58·14

i.e., Among a population of 100 4·32 cases will occur in 1st 6 months residents.
36·0 ,, ,, 1st year ,,
50·0 ,, ,, 2nd year ,,
And of 100 cases of B.W. occurring during the 2 years' period :
5·02 will occur in the 1st 6 months.
41·86 ,, ,, 1st year.
58·14 ,, ,, 2nd year.

Malaria cases	264	466	127
B.W. cases	3	22	12
B.W. rate per 100 malaria cases	1·14	4·72	9·45

i.e., For 100 cases of malaria in 1st 6 months' residents there will be 1·14 blackwater.
,, ,, ,, 1st year's ,, ,, 4·72 ,,
,, ,, ,, 2nd ,, ,, ,, 9·45 ,,
And of 100 cases of B.W. in 2 years there will be 8·05 among x malarial cases in the 1st 6 months.
33·31 ,, ,, ,, 1st year.
66·69 ,, ,, ,, 2nd year.

The next table gives the distribution of 1,050 cases of which I have found records. The data for the first six months and first year, and possibly second year, are probably fairly correct, as they have been taken from large and probably approximately equal populations. But in the third and subsequent years we do not know what proportion the population bears to that of the first year, and as I have already pointed out, this is essential before a comparison can be made. I should note, however, that Daniels in his figures has made this correction, and that the difference from the uncorrected figures was only slight.

TABLE IX.—Blackwater Fever: Effect of Residence.

First 6 months	First year	Second year	Third year	Fourth year	Fifth year	Later	Reference
1	1	4	—	1	1	3	Barratt & Yorke (1909).
?	10 (5·4 %)	42 (22·5 %)	79 (42 %)	37 (20 %)	9 (4·8 %)	?	Bérenger Féraud (1874).
2	3	2	—	1	—	—	Brem (1911).
1	2	5	6	1	1	3	Broden (1906).
?	6	22	43	20	9*	—	Burot & Legrand (1897). * Longer than 4 years.
—	—	7	1	3	—	3	Campenhout & Dryepondt (1901).
7	7	23	?	?	?	?	Cardamatis (1902).
—	8	40	12	5	1	—	Christophers & Bentley (1908).
—	1	3	3	2	5	2	da Costa (1906).
4	21	40	27	12	5	9	Daniels (1901).
39	71	79	38	12	5	4	Decks & James (1911).
—	—	—	—	—	—	1*	Howard (1907). * First attack after 24 years.
2	7	2	1	—	2	3	Koch (1899).

TABLE IX.—Blackwater Fever: Effect of Residence *continued*.

First 6 months	First year	Second year	Third year	Fourth year	Fifth year	Later	Reference
?	2	3	2*	2*	2*	39	McElroy (1905). *Six cases during 3rd, 4th, and 5th years.
—	—	13*	—	—	—	—	Mense (1899). *All had been in Africa at least 18 months.
4	10	3	3	—	—	3	Panse (1902).
12	42	41	14*	—	—	—	Plehn, A. (1903). *Later than the 2nd year.
3	9	8	4	1	—	—	Plehn, F. (1898).
?	17	?	?	?	?	?	Poole (1899).
1	2	2	—	—	—	1	Reynalds (1899).
?	5	7	28	5	2	4	Védy, cited by McElroy (1905).
76	224	346	261	102	42	75	1,126 Less 76 during first 6 months. 1,050 cases.
7·2%	21·3%	33·0%	24·9%	9·7%	4%	7·1%	

I believe that we may deduce from these figures the fact that blackwater is not a disease of the first six months or first year, but mainly of the second year. I believe this fact is capable of a simple explanation, viz., that blackwater fever only shows itself in the majority of cases when the patient has been subjected to 'repeated malarial infection lasting over a certain time.'

THE SEASONAL PREVALENCE

In Tables XA, XB the distribution of 226 European cases of blackwater fever in Northern Nigeria (1912) month by month is given. The figures have not been corrected for monthly variations in the European population as no figures are available for this purpose. From 1900-1911 the total European population has increased from about 175 to 775, but there is no reason to suppose that the increase has not been a uniform one, spread over the whole of each year, or that if in any year any disproportionate increase occurred in any particular month it would not be equalized in other months in other years.

TABLE XA.—N. Nigeria. Showing the distribution by month of blackwater cases from 1899-1911.

	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1899	10	2	1	...	...	...	...	2	2	...	1	2	20
1900	2	2	3	...	...	1	1	1	...	...	1	1	12
1901	1	...	...	...	2	1	1	2	3	...	2	...	12
1902	4	...	1	1	...	2	1	3	1	3	2	2	20
1903	...	...	1	1	...	...	2	2	3	3	2	3	17
1904	3	3	1	...	4	2	...	4	6	5	1	6	35
1905	1	...	2	...	1	1	1	3	1	3	3	4	20
1906	3	1	...	2	...	...	5	2	4	3	2	4	26
1907	...	3	2	...	1	...	1	3	...	...	...	2	12
1908	1	...	1	1	...	...	2	1	3	2	3	2	16
1909	1	2	1	2	...	1	1	2	...	1	2	1	14
1910	2	1	...	...	...	...	1	...	2	2	1	1	10
1911	2	...	1	2	...	1	2	2	1	1	...	...	12
Total	30	14	14	9	8	9	18	27	26	23	20	28	226

TABLE XB.—Northern Nigeria

Months	Actuals	Corrected for a month of 30·4368 days	Departure + or − from average 18·8
1	30	29·5	+ 10·7
2	14	15·2	− 3·6
3	14	13·7	− 5·1
4	9	9·1	− 9·7
5	8	7·9	− 10·9
6	9	9·1	− 9·7
7	18	17·7	− 1·1
8	27	26·5	+ 7·7
9	26	26·4	+ 7·6
10	23	22·6	+ 3·8
11	20	20·3	+ 1·5
12	28	27·5	+ 8·7
	226	225·5	

Column 1 represents the months. Column 2 the actuals, taken from the previous table. Column 3 the corrected figures for a month of 30·4368 days. Column 4 the departure + or — from the average figure 18·8. We observe in this table that the cases *below* the average come together, and Mr. Stott has calculated for me that it is 131 to 1 against the distribution being simply a random one. Further, he has calculated that if we take into account the *amount* of departure, that it is 1,000 to 1 in favour of the effect being due to season.

The next Tables XIA, XIB show similar figures for Southern Nigeria, Graham (1912).

TABLE XIA.—Southern Nigeria. Showing the distribution by month of blackwater cases from 1899-1911.

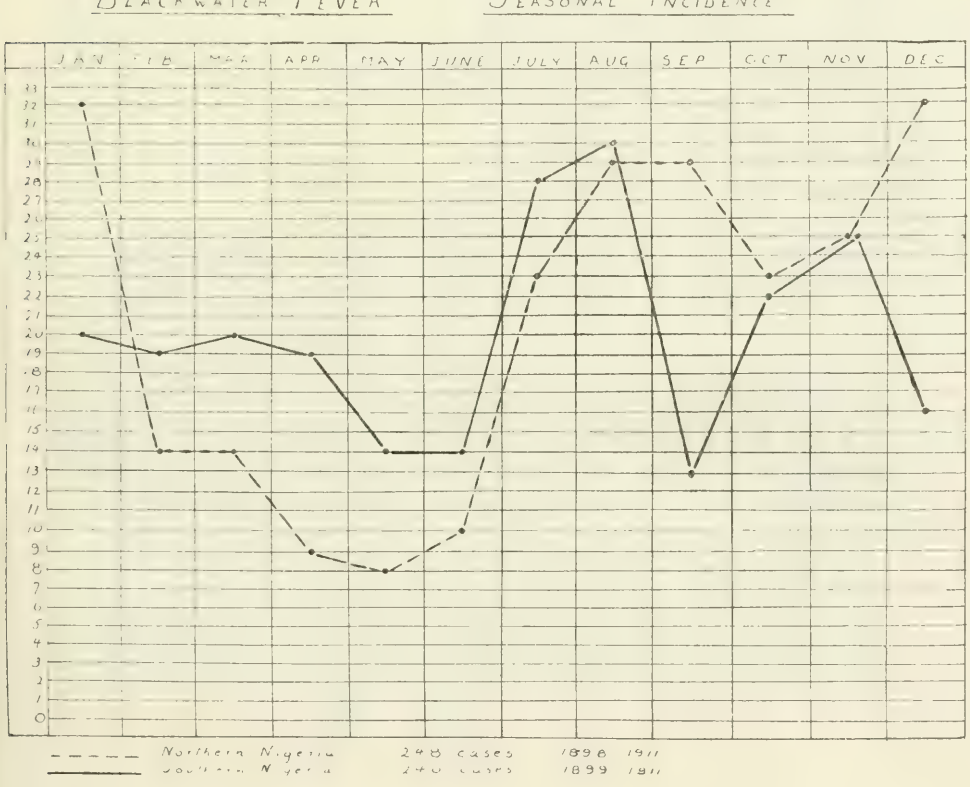
	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1899	...	...	...	...	1	...	1	2	...	...	...	1	5
1900	...	...	...	1	1	...	1	...	...	...	...	...	3
1901	2	2	...	1	1	1	2	5	1	...	3	2	20
1902	5	3	3	1	1	...	1	...	1	5	3	...	23
1903	1	1	2	2	1	2	1	3	1	1	2	1	18
1904	...	2	...	2	2	2	4	3	...	1	...	1	17
1905	1	1	2	1	2	3	...	2	...	1	...	1	14
1906	1	3	1	2	1	2	2	3	3	3	4	...	25
1907	5	...	1	1	1	1	5	3	3	1	4	2	27
1908	3	2	4	4	1	1	3	1	1	1	...	...	21
1909	1	2	2	1	...	2	1	3	2	...	...	2	16
1910	1	1	3	2	1	...	3	3	...	5	6	5	30
1911	...	3	2	1	1	...	4	2	1	4	3	1	22
Total	20	20	20	19	14	14	28	30	13	22	25	16	241

TABLE XIB.—Southern Nigeria.

Months	Actuals	Corrected figures for a month of 30·4368 days	Departure + or — from the average 20·1
1	20	19·6	— ·5
2	20	21·7	+ 1·6
3	20	19·6	— ·5
4	19	19·3	— ·8
5	14	13·7	— 6·4
6	14	14·2	— 5·9
7	28	27·4	+ 7·3
8	30	29·5	+ 9·4
9	13	13·2	— 6·9
10	22	21·6	+ 1·5
11	25	25·4	+ 5·3
12	16	15·7	— 4·4
	241	240·9	

Column 1 represents the months. Column 2 the actuals, taken from the previous table corrected for a month of 30·4368 days. Column 3 the departure + or — from the average figure 20·1. In this case Mr. Stott remarks ' some other factor seems to be at work and the probability is reduced to 7 to 1.'

CHART A



The next table represents similar figures for the European cases of blackwater admitted into Ancon Hospital.

TABLE XII.—Ancon Hospital, Panama. Showing the distribution by month of blackwater cases among Europeans from 1908-1912.

	1908	1909	1910	1911	1912	Totals	Departure + or − from the average 20
January	3	17	1	5	2	28	− 8
February ...	1	9	4	6	3	23	+ 3
March	3	10	3	4	3	23	+ 3
April	1	6	3	8	1	19	− 1
May	0	7	3	4	1	15	− 5
June	0	3	4	7	1	15	− 5
July	1	0	3	4	5	13	− 7
August	1	4	3	8	4	20	0
September ...	0	1	2	10	6	19	− 1
October	8	3	4	5	3	23	+ 3
November ...	11	7	3	6	2	29	+ 9
December ...	5	1	7	0	1	14	− 6
						241	

In Table XIII, I have given the uncorrected totals of Table XII and the totals corrected for monthly variations in the European population to show that the general conclusion is not materially affected.

TABLE XIII.—Europeans at Ancon Hospital.

	Average European Population, 1908-1912	Uncorrected		Corrected for population and for length of months		
		Blackwater cases admitted 1908-1912	Deviations from average	Blackwater rate per 10,000	Calculated to make 241	Deviations from average
1	6,061	28	+ 8	46·18	27·8	− 7·7
2	6,112	23	+ 3	37·63	25·1	− 5·0
3	6,090	23	+ 3	37·77	22·8	− 2·7
4	6,436	19	− 1	29·52	18·4	− 1·7
5	6,324	15	− 5	23·72	14·3	− 5·8
6	6,143	15	− 5	24·42	15·2	− 4·9
7	6,138	13	− 7	21·18	12·8	− 7·3
8	5,982	20	0	33·43	20·1	− 0·0
9	5,953	19	− 1	31·92	19·8	− 0·3
10	6,241	23	+ 3	36·85	22·2	+ 2·1
11	6,071	29	+ 9	47·77	29·7	+ 9·6
12	6,290	14	− 6	22·26	13·4	− 6·7
	73,841	241		392·65	241·6	
Average ...	6,153	20			20·1	

Accordingly, in Panama also, as Mr. Stott observes, we have six cases below the average coming together, making a probability of 131 to 1 in favour of a seasonal incidence, although in this case our confidence is reduced by one-third owing to the average being only over 5 years, instead of 13.

A similar conclusion can also be drawn from the figures for blackwater for all employees admitted to the Commission hospitals (Table XIV) showing that the Ancon figures are a fair sample of the conditions existing over the whole zone.

For comparative purposes the monthly distribution of malaria is also given, in which the seasonal malarial rise is clearly shown. It should be noted that there are slight discrepancies between the returns (Table XII) from Ancon Hospital (Europeans), privately communicated by Dr. James, and those given in the monthly official reports. I believe that the Ancon figures are reliable, as they are the hospital records, whereas it is easily intelligible that errors may occur in the official figures for the whole zone.

TABLE XIV.—Showing the monthly distribution of malaria and blackwater among *all* employees admitted to the Isthmian Canal Commission Hospitals, 1907-1912.

MALARIA

	1907	1908	1909	1910	1911	1912	Total	Departure from average (5,226)
January	1,822	641	1,245	479	331	496	5,014	− 212
February ...	1,607	570	832	354	375	502	4,240	− 986
March	1,570	525	657	528	402	343	4,025	−1,201
April	822	402	524	436	319	235	2,738	−2,488
May	607	393	576	613	920	257	3,366	−1,860
June	928	629	737	1,261	1,736	424	5,715	+ 489
July	1,669	1,721	944	1,750	1,971	1,035	9,090	+3,864
August	2,179	1,518	907	1,417	896	915	7,832	+2,606
September ...	1,809	1,404	963	883	651	438	6,148	+ 922
October	1,594	1,815	1,071	614	496	301	5,891	+ 665
November ...	1,019	1,447	852	558	404	272	4,552	− 674
December ...	803	1,225	763	553	385	374	4,103	−1,123
Total ...	16,429	12,290	10,071	9,446	8,886	5,592	62,714	

BLACKWATER FEVER

								(Average, 33·7)
January	3	5	13	1	8	4	34	+ 0·3
February ...	8	4	20	4	9	8	53	+ 19·3
March	6	8	9	4	5	3	35	+ 1·3
April	4	5	11	2	10	2	34	+ 0·3
May	2	4	9	7	8	2	32	− 1·7
June	2	1	6	2	9	4	24	− 9·7
July	3	4	2	7	10	2	28	− 5·7
August	2	7	2	7	11	4	33	− 0·7
September ...	2	6	7	3	13	...	31	− 2·7
October	2	7	3	5	7	...	24	− 9·7
November ...	3	13	7	3	10	...	36	+ 2·3
December ...	1	19	9	8	1	2	40	+ 6·3
Total ...	38	83	98	53	101	31	404	

TABLE XV.—Malaria among the European Troops in German East Africa.

	1893-94	1894-95	1895-96	1896-97	1897-98	1898-99	1899-1900	1900-01	1901-02	1902-03	1903-04	1904-05	1905-06	1906-07
Strength	—	123	111	104	112	105	129	130	150	162	130	138	242	189
Malaria: Cases ...	—	412	414	343	318	345	386	261	229	209	162	140	252	158
	316%	335%	373%	330%	284%	329%	299%	201%	153%	129%	125%	101%	104%	84%
Deaths ...	—	1	—	2	0	1	0	1	1	1	0	0	0	0
Blackwater Fever:														
Cases ...	—	4	32	19	30	32	19	17	12	8	9	2	6	5
Deaths ...	—	?	7	2	2	2	11	3	1	0	1	1	0	0

Most of the statistics of blackwater and malaria do not extend over a sufficiently long period to enable one to say that the correlation between the two is sufficiently close to make it fairly certain that these are connected, or both subject to the same influence. This applies, for example, to the figures for German East Africa, Schilling (1910). An examination of these figures, kindly made for me by Mr. Stott, Hon. Statistician to the School, certainly suggests a correlation, but the period of years over which they extend is too small to give a sufficiently satisfactory probability.

The next table—Table XVI—shows the amount of malaria and blackwater in Panama in blacks and whites from 1906 to 1912. All the table shows is that there has been a steady fall in malaria, and also a fall in blackwater, but one cannot argue that there is necessarily any relationship between the two, as the period is too short. Ten years hence these figures with the additional observations should be valuable. A probable fallacy is that we are not dealing with a similarly constituted population each year, owing to large emigration and immigration of labourers. If, for instance, period of residence is a factor determining blackwater, then if the number of people of each period of one, two, three, etc., years varies each year, the blackwater rate may vary quite independently of the malaria rate.

Table XVI.—Malaria and Blackwater Fever in the Panama Canal Zone.

	Employees' Annual Average			Malarial Admission Rate per 1,000 per annum			Blackwater Admission Rate per 1,000 per annum		
	Total	White	Black	Total	White	Black	Total	White	Black
1906	26,547	5,400	21,147	821·0	940·7	787·7	1·88 ?	—	—
1907	39,238	10,709	28,429	418·7	753·6	293·9	0·97	—	—
1908	43,890	12,383	31,507	280·0	507·8	190·4	1·89	5·09	0·63
1909	47,167	11,662	35,505	211·4	366·2	163·3	2·08	6·52	0·62
1910	50,802	13,021	37,781	185·9	372·7	121·5	1·04	3·07	0·34
1911	48,876	12,251	36,625	181·8	334·1	130·8	2·07	6·61	0·55
1912	50,893	12,553	38,340	109·8	216·7	74·8	0·61	1·99	0·16

But a serious drawback to this table is that the statistics regarding Americans and Europeans are massed together. The malaria and blackwater fever in these two populations, one protected, the other unprotected, or at least that does not protect itself, are entirely different, as we shall now see.

In the following figures, however, we are able to separate the data of the different races, and also we are able to do this for each month over a period of five years. The data are based on the admissions into Ancon Hospital, as in the monthly statistics for the Canal Zone no separation into races is made. The difference between the three races is briefly as follows:

(1) Americans—'gold employees'; intelligent; living in well-kept mosquito-proof houses; use of quinine at onset of fever universal; receive pay when in hospital.

(2) Europeans—Spaniards, Italians and West Indian negroes (!). Those who desire it, live in mosquito-proof houses. Neglect individual prophylaxis; indifferent to personal hygiene; *receive no pay when in hospital.*

(3) Negroes—large majority live in cheap lodging houses, or in huts; personal hygiene entirely lacking.

Now when we consider malaria and blackwater fever in these races, as represented in Chart B, we see brought out very clearly (1) that the incidence of malaria is mainly on the Europeans, much less in the Americans and still less in the Negroes. The seasonal incidence of malaria is shown very clearly in the case of Europeans and Negroes, especially in the latter years. In Americans there appears to be no clear seasonal incidence (of admissions), due no doubt to the fact that 'they universally take quinine at the onset of fever.' (2) It is precisely in the Europeans, who suffer severely from malaria, that we find blackwater, the cases being extremely few in Americans and Negroes.

Now it appears to me that the explanation is obvious, viz., that blackwater depends upon malaria. Of course it is possible to argue that the relationship depends upon the fact that we are dealing with two diseases both inoculated by the mosquito, or that those suffering from malaria are debilitated and so open to the attack of this hypothetical other disease, and even if for argument's sake we were to admit such hypotheses we should still be in the position

that this disease affects those suffering from malaria. But we consider that the obvious explanation is the true one. And again, the figures lend no support to the view that there is a quinine haemoglobinuria distinct from blackwater fever, because, if so, we should expect it in the Americans—the quinine takers.

Examining next the European admissions into Ancon Hospital for 5 years for malaria and blackwater fever, respectively, we get the results shown in Table XVII. *Statistically* there is a small but negative correlation. If now, however, we move the blackwater figures back for 4 months (i.e., make the blackwater follow the malaria 4 months later) the result seen in the third series of figures is got, and now there is a strong *positive* correlation, expressed by $r = + \cdot 50 \pm \cdot 04$ ($r = 1$ implies perfect correlation), tending to show that the two diseases are connected, for not only is there a correlation between the seasonal and secular variations which might occur, and yet not necessarily imply any connection between the two diseases at all, but there is also a coincidence between the magnitude of the oscillations of the two diseases, which, so far as the figures go, suggests that there is a real connection between the two.

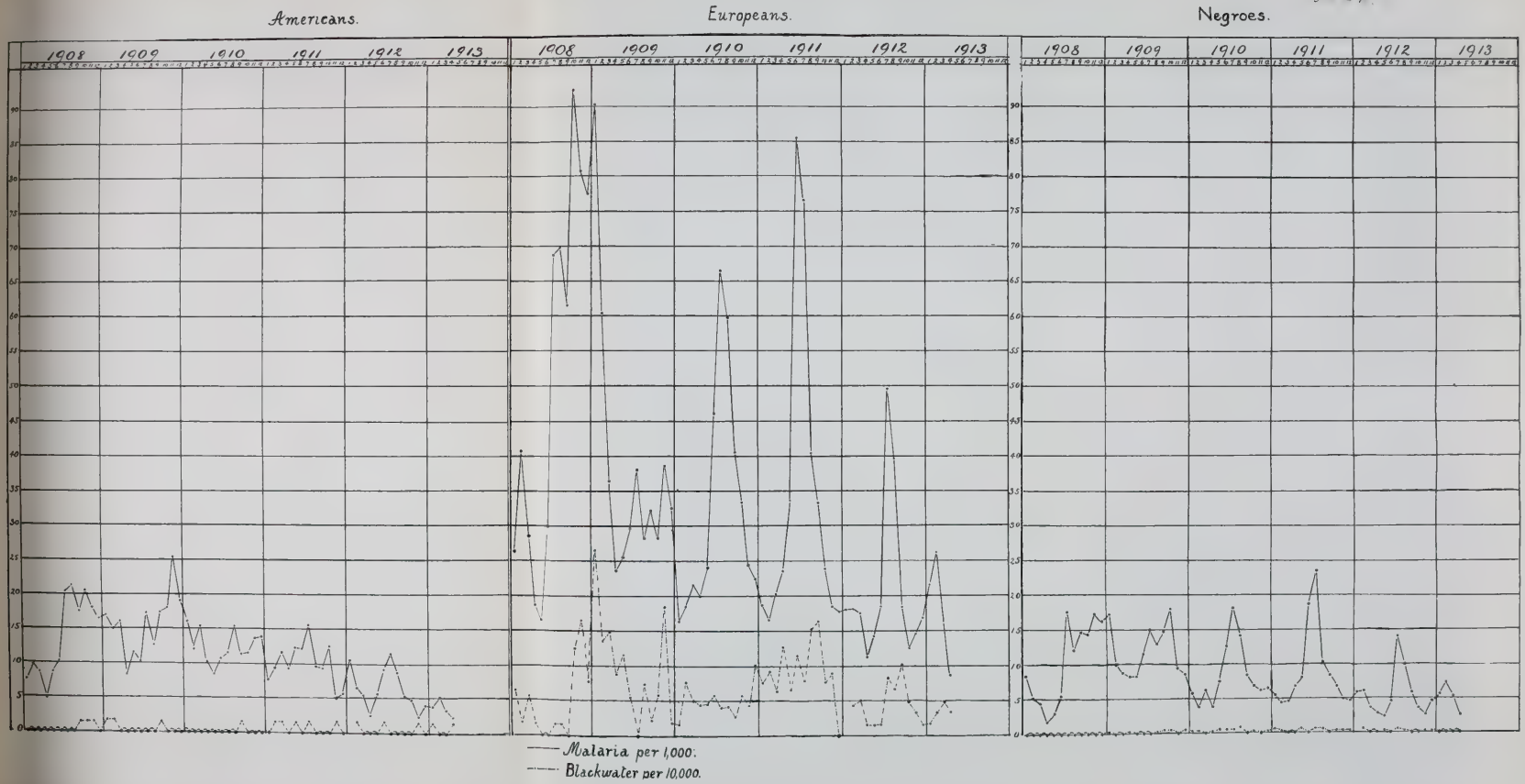
Table XVII.—Europeans, Ancon Hospital

(1) Malaria Cases

Month	1908	1909	1910	1911	1912	5 years	Departure + or − from average 1092
1	123	578	96	122	122	1,041	− 51
2	212	397	96	108	127	940	− 152
3	154	244	129	129	105	761	− 331
4	103	161	136	148	76	624	− 468
5	106	153	161	206	91	717	− 375
6	177	164	317	523	116	1,297	+ 205
7	392	213	499	441	305	1,850	+ 758
8	419	152	431	213	240	1,455	+ 363
9	344	151	298	205	109	1,107	+ 15
10	591	146	233	156	76	1,202	+ 110
11	541	146	168	125	91	1,071	− 21
12	496	172	154	119	103	1,044	− 48
	3,658	2,677	2,718	2,495	1,561	13,109	

CHART B

MALARIA AND BLACKWATER FEVER IN ANCON HOSPITAL.



(2) Blackwater Cases

Month	1908	1909	1910	1911	1912	5 years	Departure + or − from average 20
1	3	17	1	5	2	28	+ 8
2	1	9	4	6	3	23	+ 3
3	3	10	3	4	3	23	+ 3
4	1	6	3	8	1	19	− 1
5	—	7	3	4	1	15	− 5
6	—	3	4	7	1	15	− 5
7	1	0	3	4	5	13	− 7
8	1	4	3	8	4	20	0
9	—	1	2	10	6	19	− 1
10	8	3	4	5	3	23	+ 3
11	11	7	3	6	2	29	+ 9
12	5	1	7	0	1	14	− 6
	34	68	40	67	32	241	

(3) Blackwater Figures Moved Four Months Back

Month	1908	1909	1910	1911	1912	5 years	Departure + or − from average 20
1	—	7	3	4	1	15	− 5
2	—	3	4	7	1	15	− 5
3	1	0	3	4	5	13	− 7
4	1	4	3	8	4	20	0
5	—	1	2	10	6	19	− 1
6	8	3	4	5	3	23	+ 3
7	11	7	3	6	2	29	+ 9
8	5	1	7	0	1	14	− 6
9	17	1	5	2	1	26	+ 6
10	9	4	6	3	2	24	+ 4
11	10	3	4	3	3	23	+ 3
12	6	3	8	1	2	20	0
	68	37	52	53	31	241	

SECOND ATTACKS*

They occur in about 10%. I have not so far examined very extensive records. A very interesting feature about these attacks is that they are most common in the first year, and next so in the first six months. These data are, however, subject to correction for the population in each year period, but, I believe, are approximately correct. Whether this feature indicates increased susceptibility to attack, or whether they are for the most part really relapses, further consideration must show.

TABLE XVIII.—Blackwater Fever: Second attacks.

	6 months	1st year	2nd year	3rd and later years	Total
Graham (1912)	7	15	3	8	26
Christophers & Bentley (1908)	8	12	2	3	17
Deeks & James (1911) ...	8	14	2	—	16
Totals	23	41	7	11	59
Percentages ...	39	69·5	11·9	18·6	

I have to acknowledge the great kindness of Dr. James, Ancon Hospital, Panama, in supplying me with many statistical data and information on many points that arose during a consideration of the Panama figures. I also am indebted to Colonel Gorgas for similar information and interest in my work. To Mr. Stott I am indebted for the great trouble he has taken in examining my figures from the statistical point of view. Finally, I must acknowledge very gratefully the laborious work of Mr. Drawz, Bibliographer to the School, in compiling the data from the Panama Canal Commission Reports and elsewhere.

* By a second attack I mean one that has occurred *after* the discharge of the patient from hospital.

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